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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/583,996	SHAI, YECHIEL	
	Examiner	Art Unit	
	RONALD T. NIEBAUER	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 July 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22 and 43-51* is/are pending in the application.

4a) Of the above claim(s) *4-17 and 43-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,18-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/10/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants amendments and arguments filed 7/10/09 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn.

Previously (2/17/09), Applicant's elected with traverse Group 1 (claims 1-22) and the peptide species as SEQ ID NO:23.

As discussed below, the applicants elected species is obviated by the prior art. Any art that reads on non-elected species that was uncovered in the search for the elected species that reads on non-elected species is also cited herein. In accord with section 803.02 of the MPEP the claims have been examined fully with respect to the elected species and claims to the nonelected species held withdrawn from consideration.

As noted by the applicant claims 1-3,18-22 read on the elected species. Claims 4-17 read on different peptides and claims 43-51 are drawn to a different group.

Claims 4-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 2/17/09.

Claims 43-51 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 2/17/09.

Claims 23-42 have been cancelled.

Claims 1-3,18-22 are under consideration.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 7/10/09 has been considered.

Priority

This priority section appeared in the previous office action.

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/530,899 (12/22/03), fails to provide adequate written description in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

In the instant case, claims 18-21 are drawn to peptides wherein the bacterial protein is aspartate Tar receptor and peptides of specific sequences (SEQ ID NO:20,22-23).

Lack of Ipsis Verbis Support

Application No. 60/530,899 is void of support for peptides wherein the bacterial protein is aspartate Tar receptor or peptides of specific sequences (SEQ ID NO:20,22-23).

Lack of Implicit or Inherent Support

Section 2163 of the MPEP states: 'While there is no in haec verba requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure'.

Although the above statement is with respect to new claim limitations, the analysis is similar in determining conditions for receiving the benefit of an earlier filing date.

Application No. 60/530,899 recites a genus of peptides (claim 1). However, the specification does not recite SEQ ID NO:20,22-23 nor does the specification refer to embodiments in which the bacterial protein is aspartate Tar receptor.

From the disclosure of Application No. 60/530,899 there is nothing to lead one to SEQ ID NO:20,22-23 or embodiments in which the bacterial protein is aspartate Tar receptor. As such, one would not conclude that Application No. 60/530,899 provides adequate support for the instant claims.

It is noted that section 706.02 VI D of the MPEP sets forth the method to determine the effective filing date. In particular, 'If the application properly claims benefit under 35 U.S.C. 119(e) to a provisional application, the effective filing date is the filing date of the provisional

application for any claims which are fully supported under the first paragraph of 35 U.S.C. 112 by the provisional application.'. In the instant case, claims 1-3,22 are fully supported by the provisional Application No. 60/530,899. However, claims 18-21 are not fully supported by the provisional application. As such, for purposes of searching for prior art, a priority date of 12/22/04 is used for claims 18-21.

Response to Arguments Priority

Applicants argue (pages 12-14) that the essence of the present invention is the surprising finding that diasteroemeric peptides which correspond to known transmembrane domains of membrane proteins can inhibit membrane protein assembly.

Applicants argue that sequences of transmembrane domains were known in the art.

Applicant's arguments filed 7/10/09 have been fully considered but they are not persuasive.

Although Applicants argue that the essence of the present invention is the surprising finding that diasteroemeric peptides which correspond to known transmembrane domains of membrane proteins can inhibit membrane protein assembly, such argument would not lead one to SEQ ID NOs:20,22-23 of the instant invention or the subject matter of claims 18-21.

Although Applicants argue that sequences of transmembrane domains were known in the art, the relevant question is whether or not the instant claims were supported by the disclosure of the prior-filed application, Application No. 60/530,899. First, claims 18-21 are not simply drawn to transmembrane domains. Even if one considered the prior art, one would not necessarily be led to instant claims 18-21. Further, support is to be found in the disclosure of the prior-filed application, Application No. 60/530,899 not in the prior art. In fact, section 2163 of

the MPEP states: 'While there is no in haec verba requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure'. There is nothing in Application No. 60/530,899 to reasonably lead on to instant claims 18-21.

Claim Rejections - 35 USC § 112

The previous 112 2nd rejections have been overcome by the claim amendments. This 112 2nd rejection is necessitated by applicants amendments.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1,3,18-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 has been amended to recite 'consisting of: about 7 to 50 amino acid residues'. Section 2111.03 of the MPEP states that 'consisting of' excludes any element, step, or ingredient not specified in the claim. One would recognize that consisting of 7 to 50 amino acid residues would exclude 6 amino acids or 51 amino acids. However, the instant claims use the phrase 'about' in conjunction with 'consisting of'. One would recognize that 6 is about 7 and 51 is about 50. However, the phrase 'consisting of: about 7 to 50 amino acid residues' is unclear since it is unclear if 6 amino acids or 51 amino acids is included in the claim. The phrase 'consisting of' is closed terminology but the phrase 'about' is open terminology. It is unclear which phrase is controlling. There is more than one reasonable interpretation of the claims: the first interpretation

is that only 7-50 amino acids in length are included, the second interpretation is that 6-51 amino acids in length are included. For example, it is unclear if a peptide that comprises SEQ ID NO:22 of claim 21 and is 51 amino acids in length is within the scope of the claims. It is noted that dependent claims 3,18-22 do not clarify the meaning of the claims.

Claims were previously rejected under 112 1st written description. Due to the claim amendments (including the amendment to claim 19) the rejection has been updated.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3,18-20,22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107

> F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus …") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*,

the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

Further, to provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include: a) the scope of the invention; b) actual reduction to practice; c) disclosure of drawings or structural chemical formulas; d) relevant identifying characteristics including complete structure, partial structure, physical and/or chemical properties, and structure/function correlation; e) method of making the claimed compounds; f) level of skill and knowledge in the art; and g) predictability in the art.

(1) Level of skill and knowledge in the art/predictability in the art:

The level of skill in the art is high. There is unpredictability in predicting functional effects of replacements. It is not within the skill of the art to predict any and all replacements and

any and all fragments that would inhibit functional assembly of transmembrane proteins. Further, applicants arguments provides in the last paragraph of page 26 – page 27 of the reply of 7/10/09 suggests unpredictability in the art.

(2) Scope of the invention/Partial structure/disclosure of drawings:

In the instant case, the claims are drawn to diastereomeric peptides (defined on page 12) OR diasteromeric fragments, OR diasteromeric derivatives OR diasteromeric analogs. Although unclear (see 112 2nd), for purposes of examination the claims have been interpreted such that the diastereomeric peptide can be about 7-50 amino acids in length.

In considering the scope, it is first noted that claim 1 recites diastereomeric peptides (defined on page 12) OR diasteromeric fragments, OR diasteromeric derivatives OR diasteromeric analogs. With respect to the diastereomeric peptides claim 1 recites that the residues of the peptide correspond to an amino acid sequence of a transmembrane domain of a transmembrane protein. First, the claim scope is broad because no specific transmembrane protein is identified. Further the claim only requires that the peptide have an amino acid sequence of the transmembrane domain. For example, if a transmembrane domain is 10 amino acids in length, any 2 consecutive amino acids are an amino acid sequence of the transmembrane domain. One would not recognize a two amino acid sequence from the transmembrane domain of any transmembrane protein as a significant structural core.

With respect to diasteromeric fragments, diasteromeric derivatives, and diasteromeric analogs, it is noted that the only limitation is that the fragments,derivatives, or analogs comprise at least seven hydrophobic amino acid residues and that the derivative and analog comprise at least one conservative amino acid substitution. For example, if one considered SEQ ID NO:23

(the elected species, a 21 amino acid peptide) as the diastereomeric peptide, the derivatives include peptides in which the first 7 amino acids are hydrophobic the eighth amino is a conservatively substituted amino acid and amino acids 9-21 are any amino acid. Thus there are at least 20^{13} (i.e. 81920000000000000) different peptides. Further, there are many non-natural amino acids and other chemical compounds that could be considered analogs or derivatives. Further, there are many possible fragments. As such, the genus is large.

It is noted that dependent claims 2-3,18-20,22 refer to diastereomeric peptides and claim 3 specifically recites classes of proteins and claim 19 refer to SEQ ID NO:20. However, since the peptide merely needs 'an amino acid sequence', which can be any portion of the transmembrane domain, there are many peptides in the genus of claims 2-3. For example, Gly-Val are an amino acid sequence of SEQ ID NO:20. The peptide dGdGGGGGGVGGGGGGGGGGGGGGGGG comprises an amino acid sequence of the transmembrane domain and contains 2 D-amino acids. As such, the genus of peptides is large and contains no significant structural core..

The specification includes a total of 29 sequences. Such 29 sequences are not representative of the diversity of the instant claims. With respect to claim 18, the specification (page 8) recites a few sequences that appear to be from residues 13-28 of an aspartate Tar receptor. However, such peptides are not representative of any and all peptides comprising 'an amino acid sequence' of the aspartate Tar receptor. Taken together, the peptides represent a small fraction of the possible variety of peptides in the genus. One of skill in the art would not recognize that applicant was in possession of the claimed genus.

There is substantial variability in the genus. Since there are a substantial variety of componds possible within the genus, the examples do not constitute a representative number of species and do not sufficiently describe the genus claimed (see Gostelli above).

(3) Physical and/or chemical properties and (4) Functional characteristics:

Claim 1 recites that the peptide is capable of binding the transmembrane protein thereby inhibiting functional assembly. However, there is no specific disclosed correlation between structure and function. It is unclear what structural elements are required for the recited function. There are no common attributes or characteristics that identify peptides capable of binding the transmembrane protein thereby inhibiting functional assembly. As such, one of skill in the art would not recognize a core structure, common attributes, or features of the peptides. One of skill in the art would not recognize peptides capable of binding the transmembrane protein thereby inhibiting functional assembly or active fragments outside of those specifically identified. There is no teaching in the specification regarding what part of the structure can be varied while retaining the ability to bind the transmembrane protein thereby inhibiting functional assembly. In particular, no common core sequence is taught. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus and that there is a lack of the knowledge in the art regarding which amino acids can vary to maintain the function and thus that the applicant was not in possession of the claimed genus.

(5) Method of making the claimed invention/actual reduction to practice:

The specification (page 32 for example) describes the making of peptides. However, such peptides are not representative of the instant genus nor do the compounds provide a specific correlation between structure and function such that one could identify any and all peptides

capable of binding the transmembrane protein thereby inhibiting functional assembly or identify active fragments.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 1-3,18-20,22 is/are broad and generic, with respect to all possible compounds encompassed by the claims. The possible structural variations are many. Although the claims may recite some functional characteristics, the claims lack written description because there is no specific disclosure of a correlation between function and structure of the compounds beyond those compounds specifically disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. While having written description of compounds identified in the specification tables and/or examples, the specification does not provide sufficient descriptive support for the myriad of compounds embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Response to Arguments Written description

Applicants argue (pages 17-20) that the claims define a core of 7-50 amino acid residues and do not encompass a broad genus.

Applicants argue that the claims states that the fragments,analogs,and derivatives comprise at least 7 hydrophobic amino acids.

Applicants argue that the specification provides examples.

Applicant's arguments filed 7/10/09 have been fully considered but they are not persuasive.

Although Applicants argue (pages 17-20) that the claims define a core of 7-50 amino acid residues and do not encompass a broad genus, it is first noted that as claimed the diasteromeric fragments, diasteromeric derivatives, and diasteromeric analogs are not limited in length. Claim 1 recites diastereomeric peptides (defined on page 12) OR diasteromeric fragments, OR diasteromeric derivatives OR diasteromeric analogs. Further, the instant specification support amino acid extensions (page 15 lines 6-24) for the derivatives and analogs. Further, with respect to the diastereomeric peptides, claim 1 recites that the residues of the peptide correspond to an amino acid sequence of a transmembrane domain of a transmembrane protein. First, the claim scope is broad because no specific transmembrane protein is identified. Further the claim only requires that the peptide have an amino acid sequence of the transmembrane domain. For example, if a transmembrane domain is 10 amino acids in length, any 2 consecutive amino acids are an amino acid sequence of the transmembrane domain. One would not recognize a two amino acid sequence from the transmembrane domain of any transmembrane protein as a significant structural core.

Although Applicants argue that the claims states that the fragments,analogs,and derivatives comprise at least 7 hydrophobic amino acids, such information alone does not provide any specificity as to the order or arrangement of the amino acids. Further, such information does not provide a relationship between the structure and the claimed function of 'capable of binding the transmembrane protein thereby inhibiting functional assembly of said transmembrane protein'.

Although Applicants argue that the specification provides examples, the relevant question is whether or not the examples are representative of the claimed genus. For example, if one considered SEQ ID NO:23 (the elected species, a 21 amino acid peptide) as the diastereomeric peptide, the derivatives include peptides in which the first 7 amino acids are hydrophobic the eighth amino is a conservatively substituted amino acid and amino acids 9-21 are any amino acid. Thus there are at least 20^{13} (i.e. 81920000000000000) different peptides. With respect to the diastereomeric peptides claim 1 recites that the residues of the peptide correspond to an amino acid sequence of a transmembrane domain of a transmembrane protein. First, the claim scope is broad because no specific transmembrane protein is identified. Further the claim only requires that the peptide have an amino acid sequence of the transmembrane domain. For example, if a transmembrane domain is 10 amino acids in length, any 2 consecutive amino acids are an amino acid sequence of the transmembrane domain.

This 112 1st new matter rejection is necessitated by applicants amendments.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 refers to a diastereomeric fragment, diastereomeric derivative, or diastereomeric analog that comprises at least seven hydrophobic amino acid residues.

Lack of Ipsis Verbis Support

The specification is void of any literal support for 'at least seven hydrophobic amino acid residues'. Although unclear (see 112 2nd), for purposes of examination the claims have been interpreted such that the diastereomeric peptide can be about 7-50 amino acids in length.

Lack of Implicit or Inherent Support

Section 2163 of the MPEP states: 'While there is no in haec verba requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure'.

The specification (original claim 1) refer to a peptide comprising about 7 amino acid residues. However, original claim 1 does not specify that at least 7 of those amino acids be hydrophobic. The specification (page 16 lines 26-30) states that a transmembrane domain typically contains hydrophobic amino acids and states that alanine, leucine, isoleucine, proline, valine and phenylalanine are hydrophobic. A statement that a transmembrane domain typically contains hydrophobic amino acids would not lead one to peptides that contain at least 7 hydrophobic amino acids. It is noted that the term 'at least' has no upper limit. Thus, the claims

refer to derivatives and analogs in which all amino acids are hydrophobic. However, there is nothing in the specification to lead one to derivatives and analogs with all hydrophobic amino acids or at least 7 hydrophobic amino acids. It is noted that section 2163.05 III of the MPEP discusses that 'at least 35%' did not meet the description requirement because the phrase read on embodiments outside of those disclosed. In the instant case, a discussion that states that transmembrane domains typically contains hydrophobic amino acids would not lead one to specific numbers of amino acids. There is no direction provided as to how many hydrophobic amino acids are present in the derivatives, analogs, and fragments. The word 'contains' merely requires a single hydrophobic amino acid. In the instant case, the elected species (SSEQ ID NO:23) contains K,K,K,M,G,,Q,S,G,S,K,K which are not hydrophobic as disclosed in the specification (page 16 lines 26-30). There is nothing in the specification to lead one to derivatives and analogs that comprise at least 7 hydrophobic amino acids.

Hence, it can not be said that the specification provides support for 'at least seven hydrophobic amino acid residues' in the context of claim 1.

Claim Rejections - 35 USC § 101

Claim 1 was previously rejected under 101. Since the claims have been amended the rejection is updated.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 1 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The specification teach that the peptides are from naturally occurring proteins (page 4-5 connecting paragraph). Claim 1 recites diastereomeric peptides (defined on page 12) OR diasteromeric fragments, OR diasteromeric derivatives OR diasteromeric analogs. There are no specific size limitations placed on the fragments, derivatives, and analogs. The length limitations as recited in claim 1 refer to the diastereomeric peptide, not the fragments, derivatives, and analogs.

In particular, the analogs and derivatives can include any number of substitutions and deletions and are not required to have any specific number of D-amino acids. As such, the analogs/derivatives read on the naturally occurring E. coli aspartate receptor (see abstract of Melnyk et al (Biochemistry v40 2001 pages 11106-11113 as cited in IDS 9/8/08) for example). The naturally occurring E. coli aspartate receptor is a derivative of SEQ ID NO:22 which includes extensions at both the N and C-terminus (as taught by the instant specification page 15 lines 6-8) and in which the D-amino acids (dQ and dS) of SEQ ID NO:22 are substituted to L-amino acids. Thus the derivative comprises 7 hydrophobic amino acids and at least one conservative substitution as recited in the instant claim.

There is no indication that the peptides of the current invention have been isolated or removed from a naturally occurring environment. The claimed subject matter therefore reads on a product of nature.

Although unclear (see 112 2nd), for purposes of examination the claims have been interpreted such that the diastereomeric peptide can be about 7-50 amino acids in length.

Response to Arguments 101

Applicants argue (pages 21) that claim 1 recites 'consisting of' language and the peptides can not be longer than 50 amino acids.

Applicant's arguments filed 7/10/09 have been fully considered but they are not persuasive.

Although Applicants argue (pages 21) that claim 1 recites 'consisting of' language and the peptides can not be longer than 50 amino acids, Claim 1 recites diastereomeric peptides (defined on page 12) OR diasteromeric fragments, OR diasteromeric derivatives OR diasteromeric analogs. There are no specific size limitations placed on the fragments, derivatives, and analogs. The length limitations as recited in claim 1 refer to the diastereomeric peptide, not the fragments, derivatives, and analogs. The naturally occurring E. coli aspartate receptor is a derivative of SEQ ID NO:22 which includes extensions at both the N and C-terminus (as taught by the instant specification page 15 lines 6-8) and in which the D-amino acids (dQ and dS) of SEQ ID NO:22 are substituted to L-amino acids. Thus the derivative comprises 7 hydrophobic amino acids and at least one conservative substitution as recited in the instant claim. Further, it is noted that a diastereomeric derivative is not the equivalent of a diastereomeric peptide. For example, a derivative of X is not identical to X. As such, the derivatives are not limited to the length requirements of the diastereomeric peptide.

Claim Rejections - 35 USC § 102

Claim 1 was previously rejected under 102. Since the claims have been amended an updated rejection appears below.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Melnyk et al (Biochemistry v40 2001 pages 11106-11113 as cited in IDS 9/8/08).

Melnyk teach biophysical studies of transmembrane domains of integral membrane proteins (abstract). Melnyk recognizes that biophysical studies of membrane proteins has traditionally been impeded resulting in a lack of understanding of protein-protein interactions within membranes (abstract). Melnyk specifically report studies involving transmembrane segments of the E. coli aspartate receptor and other transmembrane domains and also transmembrane segments from glycophorin A (abstract). Melnyk teach the Tar-1 helix as the oligomeric determinant for the Tar protein and that the approach can be used to elucidate details of transmembrane domain folding (abstract).

Melnyk teach that the E. coli aspartate receptor transmembrane domain peptides were designed based on predictions of which residues occur in the protein transmembrane segment (see Table 2 caption). Melnyk teach that the peptides were synthesized with N and C-terminal lysines (page 11109 2nd column and Table 2). Melnyk teach the peptide KKK-VVTLLVMVLGVFALLQLISGSLFF-KKK (Tar (TM-1) 6K-Tar-1). Melnyk teach that the peptide was used in a composition (Figures 3-4 for example).

In the instant case, the peptide KKK-VVTLLVMVLGVFALLQLISGSLFF-KKK of Melnyk meets the limitation of being a diastereomeric derivative as recited in the instant claims.

In comparison to SEQ ID NO:22 are recited in claim 21, the peptide KKK-VVTLLVMVLGVFALLQLISGSLFF-KKK of Melnyk contains N and C-terminal extensions (as taught by the instant specification page 15 lines 6-8) and substitutions in which D-amino acids (dQ and dS) are substituted for L-amino acids. Thus the peptide of Melnyk comprises at least seven hydrophobic residues (for example V,V,L,L,V,V,L) and at least one conservative substitution (Q for dQ) as recited in claim 1.

Although unclear (see 112 2nd), for purposes of examination the claims have been interpreted such that the diastereomeric peptide can be about 7-50 amino acids in length.

Response to Arguments 102

Applicants argue (pages 21-23) that Melnyk does not disclose diastereomeric peptides.

Applicants argue that the claims are to diasteromeric analogs and diastereomeric derivatives which require D-amino acids.

Applicant's arguments filed 7/10/09 have been fully considered but they are not persuasive.

Although Applicants argue (pages 21-23) that Melnyk does not disclose diastereomeric peptides, instant claim 1 recites diastereomeric peptides (defined on page 12) OR diasteromeric fragments, OR diasteromeric derivatives OR diasteromeric analogs. As such, the claims are not limited to diastereomeric peptides. In the instant case, the peptide KKK-VVTLLVMVLGVFALLQLISGSLFF-KKK of Melnyk meets the limitation of being a diastereomeric derivative as recited in the instant claims. In comparison to SEQ ID NO:22 are recited in claim 21, the peptide KKK-VVTLLVMVLGVFALLQLISGSLFF-KKK of Melnyk contains N and C-terminal extensions (as taught by the instant specification page 15 lines 6-8)

and substitutions in which D-amino acids (dQ and dS) are substituted for L-amino acids. Thus the peptide of Melnyk comprises at least seven hydrophobic residues (for example V,V,L,L,V,V,L) and at least one conservative substitution (Q for dQ) as recited in claim 1.

Although Applicants argue that the claims are to diastereomeric analogs and diastereomeric derivatives which require D-amino acids, it is noted that the specification defines diastereomeric peptide (page 12 lines 17-21). However, a diastereomeric derivative is not identical to a diastereomeric peptide. For example, an insulin derivative is not identical to insulin. If the instant claims were only to diastereomeric peptides, the claims would not recite diastereomeric derivative or diastereomeric analog. The specification is clear (for example last 2 paragraphs of page 14) that the derivatives and analogs can have deletions, substitutions, and extensions. The claims do not recite that the derivatives and analogs can have deletions, substitutions, and extensions except for at the position of the D-amino acid. The specification does not define derivatives such that the derivatives must have D-amino acids. In other words, there is no specificity as to where the deletions, substitutions, and extensions (see page 14 last 2 paragraphs of the specification) of the derivatives and analogs can occur. There is no basis to exclude the deletions, substitutions, and extensions from the location of the D-amino acid.

Claim Rejections - 35 USC § 103

Claims were previously rejected under 103 based on the references cited below. Since the claims have been amended, updated rejections appear below.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3,18-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Melnyk et al (Biochemistry v40 2001 pages 11106-11113 as cited in IDS 9/8/08) and Bolognesi et al (US 5,464,933 as cited in IDS 9/8/08) and Gerber et al (JMB v322 2002 pages 491-495 as cited in IDS 9/8/08).

As discussed above, Melnyk teach biophysical studies of transmembrane domains of integral membrane proteins (abstract). Melnyk recognizes that biophysical studies of membrane proteins has traditionally been impeded resulting in a lack of understanding of protein-protein interactions within membranes (abstract). Melnyk specifically report studies involving transmembrane segments of the E. coli aspartate receptor and also transmembrane segments from glycophorin A (abstract). Melnyk teach the Tar-1 helix as the oligomeric determinant for the Tar protein and that the approach can be used to elucidate details of transmembrane domain folding (abstract). Melnyk teach that the E. coli aspartate receptor transmembrane domain peptides were designed based on predictions of which residues occur in the protein transmembrane segment (see Table 2 caption). Melnyk teach that the peptides were synthesized with N and C-terminal lysines (page 11109 2nd column and Table 2). Melnyk teach the peptide KKK-VVTLLVMVLGVFALLQLISGSLFF-KKK (Tar (TM-1) 6K-Tar-1). Melnyk teach that the peptide was used in a composition (Figures 3-4 for example).

Melnyk does not expressly teach at least 2 D-amino acids in the peptide.

Melnyk does recognize that biophysical studies of membrane proteins has traditionally been impeded resulting in a lack of understanding of protein-protein interactions within membranes (abstract). Thus Melnyk recognizes a problem in the art. Melnyk specifically report studies involving transmembrane segments of the E. coli aspartate receptor and also transmembrane segments from glycophorin A (abstract).

Bolognesi teach peptides which correspond to an HIV transmembrane protein (abstract, claim 1 for example, column 1 lines 37-39). Bolognesi specifically teach the incorporation of at least one amino acid residue in a D-isomer configuration into the peptides (claim 12).

Gerber report studies using the glycophorin A (GPA) transmembrane domain (abstract, Table 1). Gerber teach the incorporation of D-amino acids in the peptide and state that an advantage of D-amino acids is that they prevent protease degradation and result in a longer life-span of the peptide (page 494 last paragraph). Gerber teach that for the GPA analogues that all D GPA analogues exhibit the same binding affinities, insertion, and localization as the all L (page 492 last paragraph of 1st column). Gerber teach that GPA helix-helix recognition within the membrane is chirality-independent (abstract).

Melnyk does recognize that biophysical studies of membrane proteins has traditionally been impeded resulting in a lack of understanding of protein-protein interactions within membranes (abstract). Thus Melnyk recognizes a problem in the art. Melnyk specifically report studies involving transmembrane segments of the E. coli aspartate receptor and also transmembrane segments from glycophorin A (abstract). Both Bolognesi and Gerber teach what is well-known in the art – the incorporation of D-amino acids for increased stability. Further, both Bolognesi and Gerber provide the teaching for transmembrane protein fragments and in fact Melnyk even discusses the specific protein (GPA) as taught by Gerber. Since Gerber teach that an advantage of D-amino acids is that they prevent protease degradation and result in a longer life-span of the peptide one would be motivated to incorporate D-amino acid isomers into the peptide of Melnyk (i.e. KKK-VVTLLVMVLGVFALLQLISGSLFF-KKK). Since Bolognesi expressly teach the incorporation of one or more D-amino acids one would be motivated to

include any number of D-amino acids such as 2. Since Gerber teach that for the GPA analogues that all D GPA analogues exhibit the same binding affinities, insertion, and localization as the all L (page 492 last paragraph of 1st column) and teach that GPA helix-helix recognition within the membrane is chirality-independent (abstract) one would have a reasonable expectation of success.

Thus the peptide of Melnyk (i.e. KKK-VVTLLVMVLGVFALLQLISGSLFF-KKK) with multiple (for example 2) D-isomers reads on claim 1 of the instant invention. Since the peptide of Melnyk is 30 amino acids in length the limitations of claim 2 for example are met. Since Melnyk teach the peptide from E. coli aspartate receptor (abstract) the limitations of claims 3,18 are met. Since the peptide of Melnyk (i.e. KKK-VVTLLVMVLGVFALLQLISGSLFF-KKK) comprises SEQ ID NO:20 the limitations of claim 19 are met. Since the peptide of Melnyk includes KKK at both the N and C terminus, the limitations of claim 20 are met. Since the peptide of Melnyk (i.e. KKK-VVTLLVMVLGVFALLQLISGSLFF-KKK) comprises SEQ ID NO:22 the limitations of claim 21 are met. Since Bolognesi specifically teach the incorporation of at least one amino acid residue in a D-isomer configuration (claim 12) and there are a finite number of amino acids in the peptide of Melnyk it would have been obvious to optimize the location and number of D-amino acids in the peptide. Since Melnyk teach the peptide was used in a composition (Figures 3-4 for example) the limitations of claim 22 are met.

Taken together, the references teach common subject matter – peptides of transmembrane domains. Further, Melnyk does recognize that biophysical studies of membrane proteins has traditionally been impeded resulting in a lack of understanding of protein-protein interactions within membranes (abstract). The claims would have been obvious because the technique of

improving a particular class of peptides (via the inclusion of D-isomers) was part of the ordinary capabilities of a person of ordinary skill in the art in view of the teaching of the technique for improvement in other situations. In the instant case, both Bolognesi and Gerber teach what is well known in the art - the inclusion of D-isomers into peptides of transmembrane domains.

Although unclear (see 112 2nd), for purposes of examination the claims have been interpreted such that the diastereomeric peptide can be about 7-50 amino acids in length.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Claims 18-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sal-Man et al (JMB v344 2004 pages 855-864 as cited in IDS 9/8/08) and ScienceDirect web page (retrieved from http://www.sciencedirect.com/science?_ob=PublicationURL&_cdi=6899&_pubType=J&_acct=C000055109&_version=1&_urlVersion=0&_userid=2502287&md5=d82644f529ee8e69fccbfcb9d61c2f4c&jchunk=350#350 on 4/3/09 4 pages) and Bolognesi et al (US 5,464,933 as cited in IDS 9/8/08).

As discussed above (see priority section) claims 18-21 are searched based on a priority date of 12/22/04.

It is noted that Sal-Man et al is cited in the IDS 9/8/08. However, only the year is listed in the citation. ScienceDirect web page is cited to show (see page 2 left hand column) that Sal-Man et al (i.e. v344 pages 855-864) was publicly available Nov 26 2004 and thus is prior art.

Sal-Man teach peptides of the transmembrane domain of the E. coli aspartate receptor that include all L and all D versions (abstract). Specifically Sal-Man teach the peptide KKKMVLGVFALLQLISGSLKKK (Tar-1 WT Table 1) in which the peptide is either all L or all D amino acids. Sal-Man teach that the all D version has activity similar to the all L version (page 858 discussion).

Sal-Man does not expressly teach a 'diastereomeric peptide' as defined in the instant invention (page 12) to comprise L-amino and D-amino residues.

Bolognesi teach peptides which correspond to an HIV transmembrane protein (abstract, claim 1 for example, column 1 lines 37-39). Bolognesi specifically teach the incorporation of at least one amino acid residue in a D-isomer configuration (claim 12). Thus Bolognesi teach what is well known in the art.

Since Bolognesi expressly teach the incorporation of one or more D-amino acids one would be motivated to include any number of D-amino acids such as 2. Taken together one would be motivated to make the peptide of Sal-Man (KKKMVLGVFALLQLISGSLKKK) in which there are 2 D-amino acids. Since Sal-Man teach the peptide from E. coli aspartate receptor the limitations of claim 18 are met. Since the peptide of Sal-Man (i.e.

KKKMVLGVFALLQLISGSLKKK) comprises SEQ ID NO:20 the limitations of claim 19 are met. Since the peptide of Sal-Man includes K residues at both the N and C terminus the limitations of claim 20 are met. Since the peptide of Sal-Man comprises SEQ ID NO:23 the limitations of claim 21 are met. Since Bolognesi specifically teach the incorporation of at least one amino acid residue in a D-isomer configuration (claim 12) and there are a finite number of amino acids in the peptide of Sal-Man it would have been obvious to optimize the location and number of D-amino acids in the peptide.

The claims would have been obvious because a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.

Although unclear (see 112 2nd), for purposes of examination the claims have been interpreted such that the diastereomeric peptide can be about 7-50 amino acids in length.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Response to Arguments 103

Applicants argue (pages 23-29) that Melnyk does not disclose diastereomeric peptides.

Applicants argue that one would expect that incorporation of D-amino acids into a peptide would affect its helix-helix recognition.

Applicants argue that one would not expect to obtain the peptides of the claims.

Applicants state that incorporation of D-amino acid residues into the N-terminal part of DP-178 rendered the peptide inactive.

Applicants argue that the present case unexpectedly demonstrates replacing L-amino acids with D-amino acids without damaging interactions. Applicants argue that the peptides exhibit surprising and unexpected properties.

Applicants argue that they disagree with the priority date of claims 18-21 and Sal-man cannot be prior art.

Applicant's arguments filed 7/10/09 have been fully considered but they are not persuasive.

Although Applicants argue (pages 23-29) that Melnyk does not disclose diastereomeric peptides, it is noted that the instant rejection is a 103 rejection and as such any single reference does not necessarily anticipate the claims.

Although Applicants argue that one would expect that incorporation of D-amino acids into a peptide would affect its helix-helix recognition, the factual basis for such an assertion is unclear. Section 2145 I of the MPEP states that an assertion is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness.

Although Applicants argue that one would not expect to obtain the peptides of the claims and that incorporation of D-amino acid residues into the N-terminal part of DP-178 rendered the peptide inactive, it is first noted that section 2143.02 II of the MPEP states that obviousness does not require absolute predictability. Further, with respect to chemical analogues and derivatives, section 2144.09 of the MPEP (especially section 2144.09 II) states that isomers and homologs are of generally sufficiently close structural similarity that there is a presumed expectation that

such compounds possess similar properties. In the instant case, the mere substitution of D-amino acids for L-amino acids is such that the primary amino acid sequence is retained and the same side chain amino acids are present. Gerber teach the incorporation of D-amino acids in the peptide and state that an advantage of D-amino acids is that they prevent protease degradation and result in a longer life-span of the peptide (page 494 last paragraph). Gerber teach that for the GPA analogues that all D GPA analogues exhibit the same binding affinities, insertion, and localization as the all L (page 492 last paragraph of 1st column).

Although Applicants argue that the present case unexpectedly demonstrates replacing L-amino acids with D-amino acids without damaging interactions and that the peptides exhibit surprising and unexpected properties, it is unclear what is unexpected about the results. Further, with respect to chemical analogues and derivatives, section 2144.09 of the MPEP (especially section 2144.09 II) states that isomers and homologs are of generally sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. A peptide in which one or two L amino acids are changed to D amino acids are of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. Further, the art (such as Gerber page 494 last paragraph) teach that D-amino are advantageous since they can prevent protease degradation and result in a longer life-span of the peptide. Section 716.02(b) of the MPEP states that the burden is on the applicant to establish that the results are unexpected and significant.

Although Applicants argue that they disagree with the priority date of claims 18-21 and Sal-man cannot be prior art, the priority is discussed in detail in the priority section above. Briefly, Application No. 60/530,899 recites a genus of peptides (claim 1). However, the

specification does not recite SEQ ID NO:20,22-23 nor does the specification refer to embodiments in which the bacterial protein is aspartate Tar receptor. From the disclosure of Application No. 60/530,899 there is nothing to lead one to SEQ ID NO:20,22-23 or embodiments in which the bacterial protein is aspartate Tar receptor. As such, one would not conclude that Application No. 60/530,899 provides adequate support for the instant claims.

Conclusion

In the instant case, applicants amendments have necessitated new 112 2nd and 112 1st new matter rejections. The other rejections are based on previous rejections which have been updated based on the claim amendments.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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